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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,796	03/18/2004	Stewart Cole	03495.0320-01000	6307

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EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
10/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/802,796	COLE ET AL.	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-54 and 57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-54 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment After Non-final rejection filed on August 08, 2007 is acknowledged. Claims 51-54 and 57 are pending in this application. Applicant elected polypeptides encoded by ORF6 in the reply filed on December 13, 2006. The Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a)). The Restriction requirement is thus deemed proper and is made FINAL. Claims 51-54 and 57 are examined on the merits in this office action.

Julie Ha is the Examiner of record.

Maintained Rejections

35 U.S.C. 101

1. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

2. Claims 51-54 and 57 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a substantial asserted utility or a well-established utility. The specification suggests but does not demonstrate that the claimed polypeptides have GDP-D-mannose dehydratase activity based on a 51% homology with a GDP-D-mannose dehydratase from another organism. Neither the specification nor the art describe the significance of this activity or a real world use for a protein with this activity.

Response to Applicant's Arguments

3. Applicant argues that if the Office rejects claims for failing to comply with the utility requirement, it must also provide a technical reason why the rejection is being made. Applicant further argues that the Office has overlooked the specification's teachings that relate to the established utility of the claimed invention. Applicant argues that one of skill in the art would have understood the utility of the claimed invention based on the significant similarly of the polypeptide of the invention to GDP-D-mannose dehydratase, because of common knowledge in the art that variations in the polysaccharide compositions of bacterial cell walls among different species are likely due to differences in the expression of polysaccharide processing the enzyme activity, such as GDP-D-mannose dehydratase. Further, Applicant argues since the polypeptide is expressed by M. tuberculosis, but not M. bovis BCG, one of skill in the art would have understood that the polypeptide of the invention would have utility to distinguish M. bovis BCG from M. tuberculosis. Further, Applicant has submitted an excerpt from Alberts, B. et al., The Molecular Biology of the Cell (New York, NY: Garland Science, 4th ed. (2002), p. 144-145). This excerpt indicates that "generally speaking, a 30% identity in the sequence of two proteins is needed to be certain that a match has been found."

4. Applicant's arguments have been considered but have not been found persuasive because the specification does not disclose the utility of the protein, since the specification only provides that the polynucleotide of interest contains 11 ORFs that may be involved in polysaccharide biosynthesis...two of said ORFs are of particular interest namely ORF 6 that encodes a protein that shares significant homology with

bacterial DP-D-mannose dehyratases (see paragraph [0063]). The specification discloses that among the putative genes, the highest score was seen with ORF 6, whose putative product shows a 51.9% identity with GDP-D-mannose dehydratase from Pseudomonas aeruginosa (see paragraph [0238]). The translated GDP-D-mannose dehydratase sequence, GenBank Accession # U18320 (protein AAC44117.1) is a 323 amino acid residue length protein. This means that 51.9% homology of this protein would have at least 168 amino acids homologous to the wild-type. This means that there are 155 amino acid difference in sequence homology. Further, this means that there are 3100 (155*20 = 3100) different possible amino acid sequences that can encompass the 51.9% homology. Having 51.9% homology does not imply that the proteins having this homology would have same function and activity. The specification only discloses that the proteins are homologous to the GDP-D-mannose dehydratase, but has not shown that they actually function as a GDP-D-mannose dehydratase.

Rejection-35 U.S.C. 112, 1st

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 51-54 and 57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to

which it pertains or wit which it most nearly connected, to use the invention. Specifically, since the claimed invention is not supported by a substantial utility for the reason set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Response to Applicant's Arguments

7. Applicant argues that the claims are fully enabled at least because of Applicant's foregoing arguments countering the Office's rejection of the claims for allegedly failing to comply with the utility requirement. Applicant further argues that one of skill in the art would have understood that there was ample identity between the polypeptide of the invention and P. aeruginosa GDP-D-mannose dehydratase to support the expectation that the claimed peptide had dehydratase activity. Applicant provided an excerpt from Alberts, B. et al that states, "Generally speaking, a 30% identity in the sequence of two proteins is needed to be certain that a match has been found" (p. 145, lines 3-5).

8. Applicant's arguments have been considered but have not been found persuasive because having a protein sequence that is 51.9% homologous to a GDP-D-mannose dehydratase doe not mean that the homolog would have the same function and activity. It is well known in protein art that having a single difference in amino acid sequence alters the activity of the peptide. The following citations are provided since Applicant argues that having a 51.9% homology is enough to determine the protein identity and activity:

9. Rudinger (Peptide Hormones, JA Parsons, Ed., 1976, 1-7) teaches that, "The significance of particular amino acids and sequences for different aspects of biological activity cannot be predicted a priori but must be determined from case to case by painstaking experimental study" (see p. 6). Additionally, SIGMA states that with regards to design of peptide sequences that, "Even for relatively short sequences, there are essential and non-essential (or less important) amino acid residues, although the relative importance of the individual amino acid residues is not always easy to determine" (see p. 1). SIGMA further describes what effect some substitutions may have, rather than what effect they will have on hydrophobicity, secondary structure (which will affect tertiary and quaternary structure), and solubility.

10. With regards to prediction of the native conformation of a protein (structure), the art is unpredictable. Berendsen (Science, 1998, 282: 642-643) states, "The prediction of the native conformation of a protein of known amino acid sequence is one of the great open questions in molecular biology and one of the most demanding challenges in the new field of bioinformatics" (see p. 642). Furthermore, Berendsen states that "Folding to the stable native state [computationally] has not (yet) occurred, and the simulations do not contain any relevant statistics on the process. The real protein will fold and refold hundreds to thousands of times until it stumbles into the stable conformation with the lowest free energy. Because this hasn't happened (and couldn't happen) in the simulations, we still cannot be sure of the full adequacy of the force field" (see p. 642).

10. Further, the effects of a single amino acid substitution can have substantial effects on proteins in structure and/or function and are exemplified by the difference

between hemoglobin (Hb) and abnormal hemoglobins, such as sickle-cell hemoglobin (HbS). Voet et al teaches that the mutant hemoglobin HbE [GluB8(26)β to Lys] has, "no clinical manifestations in either heterozygotes or homozygotes" (see p. 235). Further, Hb Boston and Hb Milwaukee both have single point mutations which results in altered binding affinity and ineffective transfer from the Fe(III) to Fe(II) oxidation state. Conversely, a single point mutation in Hb Yakima results in increased oxygen binding by the heme core, and in Hb Kansas, the mutation causes the heme center to remain in the T state upon binding oxygen (rather than structurally rearranging to the R state) (see p. 236). Further, HbS is a single point mutation, Val to GluA3(6)β (see p. 236), which results in deformation and rigidity of the red blood cell. The mutation also provides protection against most malarial strains.

11. Given that one could not determine the structure of a protein computationally, and that the effect of amino acid substitution is unpredictable, it flows logically that one would be unduly burdened with experimentation to determine the effect of amino acid substitution(s) in a peptide or protein, with regards to structure, function, or physical/chemical properties. Therefore, making or isolating any peptide having at least 51.9% homology in amino acids that has the same activity as the claimed protein, one would be unduly burdened with experimentation to determine the effect of amino acid content, substitution(s), addition and deletions in a peptide or protein, with regards to structure, function, or physical/chemical properties.

Conclusion

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). No claims are allowed.

13. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Julie Ha
Patent Examiner
AU 1654

ANISH GUPTA
PRIMARY EXAMINER